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09/917,791	07/31/2001	Mark Dertzbaugh		9485

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EXAMINER	
GRASER, JENNIFER E	

ART UNIT	PAPER NUMBER
1645	8

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/917,791	Applicant(s) Dertzbaugh
	Examiner Jennifer Graser	Art Unit 1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Amendment, 1/2/03*

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideratio

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-7* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Priority

1. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78). This application filed under former 37 CFR 1.60 lacks the necessary reference to the prior application. A statement reading "This is a Continuation-in-Part of Application No. , filed ." should be entered following the title of the invention or as the first sentence of the specification. Also, the current status, i.e., now U.S. Patent No., of all nonprovisional parent applications referenced should be included.

Sequence Compliance

2. It is noted that page 7, Table 1, of the instant specification recites a nucleotide/amino acid sequences which are encompassed by the definitions for nucleotide sequences as set forth in 37 C.F.R. 1.821(a)(1) and (a)(2). The M.P.E.P., Section 2422.02, 37 CFR 1.821(b) requires exclusive conformance, with regard to the manner in which the nucleotide/amino acid sequences are presented and described, with the sequence rules for all applications that include nucleotide sequences that fall within the definitions. If the sequences are already in the sequence listing/CRF, then Applicants may merely amend the specification to include the appropriate sequence identifier immediately after the sequence. However, it does not appear that the sequences recited in Table 1 are contained in the Sequence Listing. APPLICANT MUST COMPLY WITH THE SEQUENCE RULES WITHIN THE SAME TIME PERIOD AS IS

GIVEN FOR RESPONSE TO THIS ACTION, 37 C.F.R. 1.821-25. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. 1.136. In no case may an applicant extend the period for response beyond the six month statutory period.

Additionally, Applicants are responsible for meeting compliance with any sequence the Examiner may have inadvertently missed.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-7 are vague and indefinite because the claims do not contain the sequence identifier which places the recited domains in relation to the entire protein. When a specific domain is identified by amino acid number, the sequence to which it refers must be included in the claims. While the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims. The claims as they stand are incomplete

and fail to provide adequate structural properties to allow for one to identify what is being claimed.

Claim 1 is vague and indefinite because it is unclear whether the polypeptide is a fusion protein or a single polypeptide

Claim 2 is vague and indefinite because it is does not appear to further limit claim 1 as nothing except the polypeptide of claim 1 is included in the "composition of matter". Do Applicants wish to claim "a pharmaceutical composition comprising one of the polypeptides of claim 1", or something else entirely?

Claim 3 is vague and indefinite because it is unclear whether or not a fusion polypeptide is being claimed.

Claim 4 is missing the word "the" before the term "A2".

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 1-7 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 6,287,566 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the patented claims limit the polypeptides to at least 100 amino acids from SEQ ID NO:21 or 22 whereas the current claims do not specify the particular sequence identifiers. The patented claims are species included in the broader genus of the claims under examination and therefore the instant claims and the patented claims are not patentably distinct from one another. .

NOTE: amendment of the current claims may constitute a statutory double patenting rejection.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Binz et al. (J.Biol.Chem, 265(16): 9153-9158. 1990).

Binz et al teach the complete amino acid sequence of the botulinum neurotoxin type A. This sequence has at least 100% identical amino acids from domains $H_{455\text{-}661}$ and $H_{1150\text{-}1289}$, i.e., Applicant's SEQ ID Nos: 21 and 22, respectively. The current claim language "having at least" is open language which encompasses the entire neurotoxin. In order to overcome the rejection the claims must be amended to recite "an isolated polypeptide *consisting of* SEQ ID NO:21 or

SEQ ID NO:22". The requirement of *at least* 100 amino acids from SEQ ID NO:21 or 22 would still read on the full-length sequence because it still allows for more than the 100 amino acids, i.e., the other 1195/6 amino acids. The composition of matter recited in claim 2 comprises only the polypeptide. This is structurally the same as the polypeptide taught by Binz et al. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

9. Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Thompson et al. (Gencore Accession NO. S09492 which corresponds to Eur. J.Biochem. 189,:73-81, 1990).

Thompson et al teach the complete amino acid sequence of the Clostridium botulinum type A neurotoxin sequence which has at least 100% identical amino acids from domains $H_{455\text{-}661}$ and $H_{1150\text{-}1289}$, i.e., Applicant's SEQ ID Nos: 21 and 22, respectively. The current claim language "having at least" is open language which encompasses the entire neurotoxin. In order to overcome the rejection the claims must be amended to recite "an isolated polypeptide *consisting of* SEQ ID NO:21 or SEQ ID NO:22". The requirement of *at least* 100 amino acids from SEQ ID NO:21 or 22 would still read on the full-length sequence because it still allows for more than the 100 amino acids, i.e., the other 1195/6 amino acids. The composition of matter recited in claim 2 comprises only the polypeptide. This is structurally the same as the polypeptide taught by Binz et al. A recitation of the intended use of the claimed invention must result in a structural

difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 3-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Binz et al J.Biol.Chem, 265(16): 9153-9158. 1990) in view of Lang (EP 562132 A1) and further in view of Lockman et al. (J.Biol.Chem. 258(22): 13722-13725, 1983).

The teachings of Binz et al are set forth above. However, they do not particularly exemplify linking said polypeptides with the A2 peptide of cholera or any other polypeptide which acts as an adjuvant.

Lang teaches antibodies to the A fragments of related tetanus toxin.

Lockman et al teach a method of fusing or joining a polypeptide with the A2 peptide of cholera toxin.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare a polypeptide comprising the neurotoxin of *C.botulinum* linked to the A2 peptide of cholera toxin because Binz and Thompson teach a detoxified botulinum toxin A which

has at least 100 amino acids from domains $H_{455-661}$ and $H_{1150-1289}$ and Lockman specifically teaches fusing a polypeptide with the A2 peptide of cholera toxin. Since Binz has suggested detoxified neurotoxin of *C.botulinum* to be a good candidate for a safe vaccine composition (see page 9153, first paragraph) and has shown that said detoxified toxin is immunogenic as demonstrated by the production of polyclonal and monoclonal antibodies (see page 9154, paragraph bridging columns 1-2) it would have been obvious to use it as a vaccine in methods of immunizing mammals susceptible to botulism. Further, since cholera toxin was a well known adjuvant/carrier at the time the invention was made, it would have been obvious to one of ordinary skill in the art to prepare polypeptide compositions or fusion proteins of *C.botulinum* neurotoxin and A2 peptide of Cholera toxin in order to provide a safe vaccine which would provide enhanced immunogenicity over a vaccine comprising *C.botulinum* neurotoxin alone. Additionally, Binz et al teach that both botulinum neurotoxin A and tetanus A fragments have similar functions (see page 9153, para. 1, lines 27-30) and Lang teaches that antibodies to A fragments of the tetanus toxin are useful for protection. The prior art teaches that most toxins are in fact protective because antibodies raised against the toxins protect from cellular effects of the toxin by binding the toxin and removing it from circulation. A detoxified toxin would be expected to be both immunogenic and protective. However, it is noted that the instant claims do not require protection. In addition, the instant toxin bears a strong degree of identity to other homologous toxins which have been found to be protective when detoxified (i.e., tetanus toxin, see page 9158, col.1, first full paragraph). The addition of A2 peptide from cholera would be

expected to enhance immunogenicity to the *C.botulinum* neurotoxin in an additive or cumulative manner.

12. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is (703) 308-4242 which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (703) 308-1742. The examiner can normally be reached on Monday-Friday from 7:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

J Graser 3/27/03

JENNIFER E. GRASER
PRIMARY EXAMINER